RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 03/11/2010, is acknowledged.

2. Claims 1, 6-8, 10-13, 15-16, 18-20, 22-46, 48, 52-56 are pending.

3. Claims 25-45 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 1, 6-8, 10-13, 15-20, 22-24, 46, 48 and 52-56 are under consideration in the instant application as they read on a method of promoting remyelination of nerve cells or reversing paralysis in a mammal comprising administering a remyelinating agent.

5. Claim 19 is objected to because it depends from canceled claims 2-4.

6. In view of the amendment filed on 03/11/2010, only the following rejections are remained.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1, 6-8, 10-13, 15-20, 22-24, 46, 48 and 52-56 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-7, 11-13, 28 and 29 of copending Application No. 11/540,640 for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicant points to MPEP § 804(I)(B) which indicates that a provisional OTDP rejection over another application should be made unless the provisional double patenting rejection is the only rejection remaining in at least one of the applications. In the present instance, the other application 11/540,640 was filed after the present application. Because the claims in the present application are otherwise allowable as discussed below, the Examiner should withdraw the provisional OTDP rejection in the present case and allow it to issue.

However, OTDP is not the only rejection remaining in the instant application. Accordingly, the rejection is remained.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e1) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

10. Claims 1, 6-8, 10-13, 15-20, 22-24, 46, 48 and 52-56 stand rejected under 35 U.S.C. 102(a)/(e) as being anticipated by US 20070025989 (102(e)) or WO/2003/072040 for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicant notes that US Publ. No. 2007/0025989 is application no. 11/540,640 cited in the obviousness double patenting rejection above. The inventors in application no. 11/540,640 and W0/2003/072040 were under an obligation to assign the invention to the Assignee of the present application and as such the disclosure of US Publ. No. 2007/0025989 is not work by "another." Thus, US Publ. NO. 2007/0025989 and WO/2003/072040 is not prior art to this application

under 35 U.S.C. 102(a)/(e). Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

Contrary to Applicant's arguments, the MPEP 2136.04 states "another" means other than applicants, *In re Land*, 368 F.2d 866, 151 USPQ 621 (CCPA 1966), in other words, a different inventive entity. The inventive entity is different if not all inventors are the same. The fact that the application and reference have one or more inventors in common is immaterial. *Ex parte DesOrmeaux*, 25 USPQ2d 2040 (Bd. Pat. App. & Inter. 1992) (The examiner made a 35 U.S.C. 102 (e) rejection based on an issued U.S. patent to three inventors. The rejected application was a continuation-in-part of the issued parent with an extra inventor. The Board found that the patent was "by another" and thus could be used in a 35 U.S.C. 102 (e)/103 rejection of the application.). In the instant case, the instant Application has 9 inventors and the `989 publication and `040 publication have only two inventors. It is not even clear from the record whether the inventor Ted Yednock in the instant application is the same Theodore Yednock in the `989 and `040 publications. Accordingly, both `989 and `040 publications qualify as art under 35 U.S.C. 102 (e)/(a) as by another.

11. Claims 1, 6-8, 10-13, 15-16, 46, 48 and 52-56 stand rejected under 35 U.S.C. 102(a) as being anticipated by Miller et al (N Engl J Med. 2003 Jan 2;348(1):15-23) for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicant submits that Miller reports the results of a controlled trial of natalizumab for relapsing multiple sclerosis. Miller administers natalizumab or placebo every 28 days for 6 months and states that the subjects had fewer brain lesions and fewer relapses than untreated patients. But Miller indicates that the treated patients were still developing new brain lesions and still displayed relapses and the combined values obtained at month 9 and month 12 showed that the number of new enhancing lesions and scans showing activity were similar in all the groups, those receiving the placebo, 3mg/kg natalizumab or 6mg/kg natalizumab. Thus while the Miller treatment regimen may have slowed an aspect of disease progression, Miller does not teach a method that promoted remyelination or reversal of paralysis. Therefore, Miller does not teach Applicants' method for promoting remyelination of nerve cells by chronically administering an antibody that binds to alpha-4 beta-1 integrin, e.g., natalizumab, in a remyelinating effective amount weekly or monthly over a period of at least 6 months, or at least one year as recited in claims 18 and 56. As such Miller does not anticipate the invention as claimed.

However, it is noted that the CAFC held in Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc., 58 USPQ2d 1508 (CA FC 2001) that when a claimed process is not directed to a new use, *consists of the same steps described in a prior art reference*, and the newly discovered results of the known process *directed to the same purpose* are inherent, the process is not patentable. In

the instant case, promoting remyelination/reversing paralysis are inherent properties of the referenced method.

12. Claims 1, 6-8, 10-13, 15-16, 18-20, 22-24, 46, 48 and 52-56 stand rejected under 35 U.S.C. 102(a) as being anticipated by National Horizon Scanning Centre article (July 2002) for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

In addition to Applicants' remarks already of record, Applicants note that National Horizon summarizes results that were presented on the Elan Corporation's website www.elan.com/research/antegren.asp Accessed April 16, 2002 (see National Horizon page 3 after "Effectiveness" reference number 6) and states that patients with relapsing-remitting MS or secondary progressive MS received either iv natalizumab (3mg/kg or 6mg/kg) or placebo every 4 weeks for 6 months. As such the results presented on the Elan Corporation's website and cited in National Horizon is not "work by another" and does not qualify as prior art under 35 U.S.C. 102(a)
The Examiner also cites National Horizons' discussion of the results of Tubridy et al., already of record (see National Horizon page 3 after "Effectiveness" reference number 7.) In particular, National Horizons cites Tubridy's report that the patients received only two iv infusions of natalizumab or placebo 4 weeks apart and then followed for up to 24 weeks with serial MRI and clinical assessment. Tubridy did not disclose chronically administering natalizumab monthly or weekly for at least 6 months, or at least a year as recited in claims 18 and 56 and therefore does not anticipate the invention as currently claimed.

However, it is noted that the National Horizon Scanning Centre article was published July 2002 while Applicant's claimed priority is Jan. 2003. Accordingly, National Horizon Scanning Centre reporting is qualified as another's prior knowledge. It has been held that another's prior knowledge or use is prior art under section 102(a) if it was accessible to the public. See *Carella V. Starlight Archery*, 231 USPQ 644 (Fed. Cir. 1986). National Horizon Scanning Centre's reporting was accessible to the public. Applicant did not disqualify National Horizon Scanning Centre as another's prior knowledge. See MPEP 2132.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 6-8, 10-13, 15-16, 18, 46, 48 and 52-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Tubridy et al (Neurology, 1999 Aug 11;53(3):466-72) for the same reasons of record.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicants disagree with the Examiner's previous position with respect to the issue of long-felt need. Applicant submits that prior to Applicant's teaching no other treatment, even treatments that reduced inflammation, produced the remyelinating effects obtained by Applicants' method as claimed. Thus one of skill in the art based on the prior art of record at the time of this invention would not have expected a chronic natalizumab treatment method to promote remyelination. Tubridy et al. does not suggest the steps of Applicants' method as claimed and in fact teaches away for Applicants' method steps by stating that while there were significant differences at 12 weeks, such was not the case at 24 weeks and that the relatively modest correlations between disability and changes seen on MRI means that any potential new treatment must ultimately be tested in a larger longer term trial. Tubridy states:
"to obtain adequate serum concentration of Antegren [natalizumab] between monthly infusions and to maintain suppression of MRI activity, a higher dose of Antegren administered chronically will need to be evaluated in future studies. It is possible, however, that repeated dosing with a mAb could lead to anti- idiotype antibodies and if of sufficient magnitudes, a loss of efficacy. Further studies are needed to determine more accurately the magnitude and duration of the effect of Antegren on MRI. Thus Tubridy et al. is only suggesting further experimentation, not the particular steps of Applicants's method as claimed and as such fails to render the claimed invention obvious.

However, it remains the Examiner's position that those skill in the art would have had reason to chronically administer the anti-α4 antibody of Tubridy to evaluate the effect of anti-α4 integrin antibody on brain lesion activity in MS. Any measurable correlations between disability and changes seen on MRI is considered improvement. There is clear and explicit suggestion in Tubridy et al to use a higher dose of Antegren (natalizumab) administered chronically will need to be evaluated in future studies (see page 471, 2nd col., 2nd full ¶). Given that natalizumab treatment was well tolerated and show shot-term treatment results in a significant reduction in the number of new active lesions on MRI, one of ordinary skill in the art would have had a reasonable expectation of success of chronically treating multiple sclerosis according to the teachings of Tubridy by providing an anti-α4 antibody to a patient suffering from this disease inasmuch as the reference discloses that such agents are well tolerated to treat MS and further

studies to determine the longer term effect (chronic administration)) of this treatment on MRI and clinical out comes.

15. Claims 1, 6-8, 10-13, 15-16, 18, 46, 48 and 52-56 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299 in view of Tubridy et al (Neurology, 1999 Aug 11;53(3):466-72) for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

The '299 Patent does not teach the chronic administration of the antibody over a period of at least 6 months or at least 1 year and is silent regarding "remyelination of nerve cells" and "reversing paralysis." Furthermore, Tubridy teaches that at 24 weeks after patients received two IV administration of anti-α4 integrin antibody 4 weeks apart there were no significant difference in the number of new active or new enhancing lesions between the groups of treated and control patients. Thus Tubridy only teaches a regimen that may slow progression of the disease, but there is no teaching or suggestion of a regimen that would promote remyelination or reverse paralysis. Thus one of skill in the art considering the '299 Patent in combination with Tubridy would not expect that the chronic administration of natalizumab over a period of at least 6 months, or at least a year for claims 18 and 56, would promote remyelination and reverse paralysis.
One of skill in the art evaluating the '299 Patent and Tubridy in combination and in the context of the state of the art at the time of filing, and considering that prior to Applicants' invention no treatment regimen had ever produced remyelination or reversal of paralysis, would not have reasonably expected and would be surprised that the chronic administration of a remyelinating amount of an anti-a4 integrin, e.g., natalizumab, would promote remyelination and reversal of paralysis.
The combination of the '299 Patent and Tubridy fail to render the invention as currently claimed obvious and Applicants request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. 103(a).

However, it remains the Examiner's position that the claimed properties of "remyelination of nerve cells" and "reversing paralysis" are considered inherent property of a method for treating multiple sclerosis by chronically administering natalizumab. The claims purport to be a method for "promoting remyelination of nerve cells" is an old therapy with the inherent results of the old therapy. With respect to applicant's arguments concerning the remyelination effect of the natalizumab according to the claimed method, although the reference teachings do not explicitly teach the same mechanism of nerve remyelination, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). Also, regarding process claims, a preamble recitation that merely expresses the purpose of performing the claimed steps is not a limitation on the process where the body of the claim fully sets forth the steps required to practice the claimed process, and where the preamble

recitation does not affect how the claimed steps are to be performed. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001).

16. Claims 1, 19-20 and 22-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,840,299, each in view of Tubridy et al, and further in view of U.S. Pat. No 6,753,135 for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicant points that the Examiner states that the '135 patent teaches prednisone is a corticosteroid used to treat a wide variety of inflammatory disorders including multiple sclerosis. However, Applicants submit that despite the long history of prednisone use, it is not known to promote remyelination. The '299 Patent and Tubridy et al. do not disclose Applicants' discovery that chronic administration of natalizumab, surprisingly, is useful for promoting remyelination. Therefore at the time of this invention based on the teaching of the cited art one of ordinary skill in the art would not combine prednisone with natalizumab in a method to promote remyelination. As such, the combination of the '299 Patent, Tubridy and the '135 Patent fails to render Applicants' invention as claimed obvious.

However, the reason to combine may often suggest doing what the Appellant has done, but for a different purpose or to solve a different problem than that asserted by the Appellants. "It is not necessary in order to establish a *prima facie* case of obviousness… that there be a suggestion or expectation from the prior art that the claimed monovalent GP1b antibody fragments will have the same or a similar utility as one newly discovered by the applicant (emphasis added). See In re Dillon, 919 F.2d 688, 692, 16 USPQ2d 1897, 1900 (Fed. Cir. 1990). Thus, it is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144. That is rationale different from Applicant's is permissible. In the instant case, the `135 patent teaches that prednisone is a corticosteroid used to treat a wide variety of inflammatory disorders, including multiple sclerosis, it would have been obvious to one of ordinary skill in the art at the time the invention was made to co-administer prednisone taught by the `135 patent with anti-VLA-4 antibodies taught by the ` '299 patent in view of Tubridy et al in a method of chronically treat multiple sclerosis.

17. Claims 1, 19-20 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al, and further in view of U.S. Pat. No 6,753,135 for the same reasons set forth in the previous Office Action mailed 09/11/2009.

Applicant's arguments, filed 03/11/2010, have been fully considered, but have not been found convincing.

Applicant's arguments and the examiner's rebuttal are essentially the same as set forth above in Section 16.

18. No claim is allowed.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 22, 2010

/Maher M. Haddad/
Primary Examiner,
Art Unit 1644